Board of Pharmacy

Final Statement of Reasons

Subject Matter of Proposed Regulation: Compounding Definitions

Title 16 Sections Affected: Amend 16 Cal. Code Reg. § 1735.1, 1735.2, 1735.3 and 1751.2

Updated Information

The Initial Statement of Reasons is included in this rulemaking file. The information contained therein accurately reflects the board's position regarding the adoption of the above sections, but is updated to include the following information.

The Board of Pharmacy conducted a regulation hearing on May 1, 2012. At its public Board Meeting held May 1, 2012, the board considered the comments received during the 45-day public comment period, as well as the comments received at the regulation hearing. The Board's responses to the comments received are detailed under "Summary of Comments Received during the 45-Day Comment Period and Regulation Hearing." After reviewing the comments received during the 45-day comment period and regulation hearing, the Board directed staff to take all steps necessary to complete the rulemaking process, authorize the Executive Officer to make any non-substantive changes, and authorize staff to send out a 15-day modified text notice that includes changes discussed and voted on at the May 1st meeting. The board further directed that if no adverse comments were received during the 15-day comment period, authorize the Executive Officer to adopt the regulations at Sections 1735.1, 1735.2, 1735.3 and 1751.2 as noticed in the modified text Notice.

The Notice issued by the board on July 5, 2012, noticed the public of the 15-day public comment period of modified text. In that same notice, and in accordance with Section 11347.1 of the Government Code, the board provided notice of the document identified below being added to the rulemaking record. This document is incorporated by reference at § 1735.3(a)(6). The board did not receive any comments in response to the notice related to the addition of this document to the rulemaking record. It is noted that the document added is published by the United States *Pharmacopeial* Convention. However, the term "United States Pharmacopeia" or "USP" are common terms used throughout the rulemaking.

The following changes were made to the form incorporated by reference at 16 CCR § 1735.3 (17M-39), which are deemed to be non-substantive:

Form 17M-39

On page 9, item 13.1.4, the board modified the text of the label for cytotoxic products to read "Cytotoxic – Dispose of Properly." This language was changed to reflect the language approved by the board as reflected in the modified text made available for 15 days (July 5-20, 2012).

On page 11, item 15.5, a Title 24 citation was updated to read "505.5.1" (not 505.12.1). In the 2010 Triennial Adoption Cycle, the Building Standards Commission moved sections applicable to Pharmacies-Compounding Area of Parenteral Solutions (Sections 505.5 and 505.5.1) within Title 24, Part 4, Chapter 5. The content of the sections was not altered; only the section numbers were changed. This change is being made so that pharmacies that must complete the Compounding Self-Assessment Form (17M-39) will have an accurate reference for sections relative to pharmacies.

Local Mandate:

None.

Business Impact:

This regulation will not have a significant adverse economic impact on businesses. This determination was based on the absence of comments or testimony indicating adverse economic impact regarding this rulemaking proposal.

Specific Technologies or Equipment:

This regulation does not mandate the use of specific technologies or equipment.

Consideration of Alternatives:

No reasonable alternative which was considered would be more effective in carrying out the purpose for which the regulation was proposed, would be as effective and less burdensome to affected private persons than the adopted regulation, or would be more cost effective to affected private persons and equally effective in implementing the statutory policy or other provision of law.

Summary of Comments Received During the 45-Day Comment Period and at the Regulation Hearing Held May 1, 2012 (Objections or Recommendations/Responses):

The board received the following comments during the 45-day public comment period. A summary and response is also provided for comments received at the Regulation Hearing held May 1, 2012.

<u>Comment from Kevin Brown, Pharm D.</u>

Dr. Brown commented on record keeping requirements for compounded and sterile-injectable compounded drug products. Though not explicitly stated, the board believes that Dr. Brown's comments were directed to the board's proposal at 16 CCR 1735.3(a)(6), where the 'expiration date' of each component in a compounded drug product is required to be documented in the pharmacy record. Though Dr. Brown indicates in his letter that a

pharmacist checks 'beyond use dating' (i.e. expiration date) for each component while compounding, Dr. Brown stated added documentation reduces safety to the patient because of increased complexity in the process of compounding. The board rejected this comment. The recording of a components expiration date would aid in the proper labeling of the (final) drug product that is dispensed to a patient and could help prevent an expired medication from reaching a patient for administration.

Dr. Brown asked the board to consider fundamental differences between batching IV compounded drug products for future use, and compounding patient-specific injectable compounded drug products, and asked that *all patient-specific compounded drug products be exempt from regulation*. He specifically stated his objection to the board's proposal to require added documentation for patient-specific compounded medications.

Current regulations at Article 4.5 (compounding) and Article 7 (sterile injectable compounding) provide existing requirements for compounded and sterile injectable compounded drug products. Existing regulations at Articles 4.5 and 7 specify requirements for facilities, policies and procedures, record keeping, compounding attire, quality assurance and process validation, training of staff, etc. Existing regulations provide necessary patient protections so that compounded drug products are safe for patients. To exempt all patient-specific compounded drug products from board regulation could put patients at considerable risk. Further, existing regulation at § 1753.3 exempts from specified documentation (including the requirement to document the expiration date of each component) those sterile products compounded on a one-time basis for administration within seventy-two hours. To maintain patient protection for compounded drug products, the board rejected the comment opposing the documentation of the 'expiration date' of each component of a compounded drug product.

Dr. Brown spoke in support of the requirement to identify the lot number in the record for batched compounded drug product. The board appreciates Dr. Brown's comment.

Comment from Charles Daniels, RPh

Mr. Daniels comments were rejected by the board, as the comments were not relevant to the board's proposal or to the procedures followed by the board in proposing or adopting the action. Specifically, Mr. Daniels commented on various Title 16 sections that were not a part of the board's rulemaking.

Comments from Steven Gray, PharmD, JD

Dr. Gray commented in support of the board's proposal to add a definition of "equipment" as proposed at § 1735.1. The board appreciates Dr. Gray's comment.

Dr. Gray commented in support of the board's proposal that removes from the 'pharmacy record' the "equipment to be used" and – instead – requires the written master formula record to specify this information. The board appreciates Dr. Gray's comment.

Dr. Gray commented in support of extending the time (to 72 hours) for which sterile products compounded on a one-time basis, as specified, is exempt from the documentation requirements at § 1735.3(a)(6). The board appreciates Dr. Gray's comment.

Dr. Gray commented in support of modifying the label requirements of cytotoxic drug products as specified at § 1751.2. The board appreciates Dr. Gray's comment.

Dr. Gray asked that the board specify at § 1735.3(a)(6) the specific USP 797 reference related to "redispensed CSPs." In response to this comment, the board modified the language at § 1753.3(a)(6) to incorporate by reference *United States Pharmacopeia Standards for "Redispensed CSPs" in Chapter 797 (35th Revision, Effective May 1, 2012),* and issued the modified text for a 15-day public comment period.

At the regulation hearing held May 1, 2012, Dr. Gray spoke in support of the board's rulemaking and reiterated his request to specify USP 797 related to "redispensed CSPs."

Comments from Katy Marconi, PharmD

Dr. Marconi commented on the board's regulatory history related to compounding, referenced the scope of services provided in the profession of pharmacy related to compounding, commented on hospital inspections made by other entities, commented on appropriate actions regarding drug recalls, and other topics that were not specifically directed at the board's proposed action or to the procedures followed by the board in proposing or adopting the action. The board rejected these comments.

Dr. Marconi commented that the board's regulations go above and beyond the recognized compounding standards that are found in USP 797 and that she takes issue with board regulations in various areas. The board rejected this comment as there is no comment specifically directed at the board's proposed action (proposed text) or to the procedures followed by the board in proposing or adopting the action.

Dr. Marconi objected to documenting the 'equipment used in compounding' as it is not addressed in USP 797. Current board regulation (§ 1735.3) requires that the "equipment" used in compounding a drug product be specified in the "pharmacy record." The board rejected this comment as documenting the 'equipment used' in compounding a drug product is a current requirement, and the board's proposal moves this requirement to documenting the "equipment used" in the "written master formula record"(at § 1735.2) instead.

Dr. Marconi commented that she took 'issue' with board regulations that require quality assurance assessments. The board rejected this comment. The board's requirements related to quality assurance assessments are found at Title 16 § 1751.7 and are not a part of this rulemaking.

Dr. Marconi commented that she has no issue with the labeling of cytotoxic compounded items. The board infers this comment is in support of the board's proposal at § 1751.2.

Dr. Marconi commented on the board's proposal requiring the documentation of the expiration date of each component in a compounded drug product, adding that if recalls need to be addressed, that should be done in an area of regulation specific to drug recalls. The board disagrees with and rejects this comment because recording the expiration date of each component in a compounded drug product will aid in the proper labeling of the drug product prior to dispensing to a patient. Existing regulation at § 1735.2(h) requires

every compounded drug product to be given an expiration date representing the date beyond which the drug product shall not be used. This 'beyond use date' shall not exceed the shortest expiration date of any component in the compounded drug product, with certain exceptions. Thus, the board's proposal to require that the pharmacy record include the expiration date for each component in a compounded drug product will aid in the proper labeling of the drug product. The board also asserts that this requirement provides an added check to prevent expired medication from reaching patients and that it would allow for traceability and accountability for the compounded drug product.

Dr. Marconi commented on the board's proposal (at § 1753.3(a)(6)) which exempts from recording the expiration date (and other information) for sterile products compounded on a one-time basis for administration, as specified, stating the board's proposal is unnecessary. The board disagrees with this comment.

Dr. Marconi commented that hospitals that engage in sterile-to-sterile compounding should adhere to USP 797 standards (inferred, USP *only*). Also, Dr. Marconi comments/suggests that when a pharmacy engages in non-sterile to sterile compounding, adherence to USP 795 and USP 797 should be enforced. The board rejected these comments. The board has promulgated regulations related to all compounding (Title 16 Article 4.5) and additional regulations related to sterile compounding (Title 16 Article 7) that provide for patient safety and consistency in the compounding of prescription drug products that are administered or dispensed to California patients. These regulations apply to the compounding of prescription drug products by *any* pharmacy that prepares prescription drug products to be administered or dispensed to California patients – including hospital pharmacies.

At the regulation hearing held May 1, 2012, Dr. Marconi expressed her concern regarding the progression of the rulemaking. She referenced her written comments and stated that she does not support addressing compounding globally. She stated her recommendation that sterile-to-sterile compounding be conducted according to USP 797 and stated that the board's rulemaking should only apply to non-sterile to sterile compounding. The board disagreed with Dr. Marconi's broad statement and rejected the comment. Dr. Marconi spoke about drug recall issues, which are unrelated to the board's proposed action.

Comments from Kent Martyn, PharmD

Dr. Martyn made general comments on the differences between hospital, retail, and compounding pharmacies; he commented on topics that that were not relevant to the board's proposal or to the procedures followed by the board in proposing or adopting the action. The board dismissed/rejected these comments.

Dr. Martyn comments that "adding lot # requirements" will not affect patient care when it comes to recalls. Existing regulation at 16 CCR § 1735.3(1)(6) requires that the pharmacy record include the lot number of each component for a compounded drug product. The board did not propose any changes to that requirement and rejected the comment.

Dr. Martyn states "There is no need for 'artificial' dating to be applied by the Board." It is unclear to the board what Dr. Martyn is asserting. He further makes a comment that sterile-to-sterile compounds should not be subject to additional bookkeeping requirements. The board's

proposal at 16 CCR § 1753.3(a)(6) would require that the "expiration date" of each component of a compounded drug product be recorded in the pharmacy records. This is not an artificial date; it is the expiration date of one component (ingredient) of a compounded drug product. The board disagrees with and rejects this comment because recording the expiration date of each component in a compounded drug product will aid in the proper labeling of the drug product prior to dispensing to a patient. Existing regulation at § 1735.2(h) requires every compounded drug product to be given an expiration date representing the date beyond which the drug product shall not be used. This 'beyond use date' shall not exceed the shortest expiration date of any component in the compounded drug product, with certain exceptions. Thus, the board's proposal to require that the pharmacy record include the expiration date for each component in a compounded drug product will aid in the proper labeling of the drug product. The board also asserts that this requirement provides an added check to prevent expired medication from reaching patients and that it would allow for traceability and accountability for the compounded drug product.

Dr. Martyn provided a general comment that "adding more steps to a process induces errors." It is unclear to the board what 'added steps' Dr. Martyn is referring to or if the comment is directed at the board's proposed action. The board dismissed/rejected this comment.

At the regulation hearing held May 1, 2012, Dr. Martyn commented on "reasonable quantity." The board rejected this comment as it is not directed at the board's proposed action. Specifically, the definition of "reasonable quantity" is specified at 16 CCR § 1735.2(c), and the board did not propose any changes to this section in its rulemaking. Dr. Martyn also commented on the "72-hour" reference at proposed § 1735.3(a)(6), adding that this requirement conflicts with the board's existing regulation at § 1735.2(h) related to 'beyond use date.' He stated that the board's proposal will have a significant financial impact on labor costs and the cost of materials, but did not provide any specificity as to what impact or cost would be realized. The board disagrees with and rejected Dr. Martyn's comment that the board's proposal at § 1735.3(a)(6) conflicts with the board's existing regulation at § 1735.2(h) related to 'beyond use date.' The board's proposal at § 1753.3(a)(6) specifies what information is exempt from recording in a pharmacy record for sterile products that are compounded on a one-time basis for administration to an inpatient within 72 hours in a health care facility, as defined. The board's existing regulation at § 1735.2(h) specifies that a pharmacy's written master formula record for a compounded drug product specify 'beyond use dating' as required by § 1735.2(h). This written master formula record is required to be included in the pharmacy's records for each compounded drug product (see existing regulation at § 1735.3(a)(1)).

Comments from Kristin Niemi, PharmD

Dr. Niemi made general statements regarding the negative safety impact the board's existing compounding regulations have on patient-specific IV (sterile) compounded products in the inpatient setting. Dr. Niemi asks the board to consider the fundamental differences between batching IV compounded drug products for future use, and preparing patient-specific sterile injectable compounded drug products. The comment(s) were not relevant / specific to the board's proposal (proposed text) or to the procedures followed by the board in proposing or adopting the action; thus, the comments were dismissed/rejected by the board.

Dr. Niemi commented in opposition to adding "extra steps of product documentation" and that the board's proposal provides no value to a specific product that is being produced for a specific patient. The board infers that this comment is directed at its proposal to amend § 1753.3(a)(6) where the expiration date would be required to be recorded in the pharmacy record for every component (ingredient) in a compounded drug product. The board disagrees with and rejects this comment because recording the expiration date of each component in a compounded drug product will aid in the proper labeling of the drug product prior to dispensing to a patient. Existing regulation at § 1735.2(h) requires every compounded drug product to be given an expiration date representing the date beyond which the drug product shall not be used. This 'beyond use date' shall not exceed the shortest expiration date of any component in the compounded drug product, with certain exceptions. Thus, the board's proposal to require that the pharmacy record include the expiration date for each component in a compounded drug product will aid in the proper labeling of the drug product. The board also asserts that this requirement provides an added check to prevent expired medication from reaching patients and that it would allow for traceability and accountability for the compounded drug product.

Comments from Richard Sakai, PharmD

Dr. Sakai made general comments on topics that were not specifically directed at the board's proposed action or to the procedures followed by the board in proposing or adopting the action. The board rejected these comments. Dr. Sakai asserts that the board's proposal would require his organization to purchase a Robotic Intravenous Admixture machine. The board did not propose that specified technology be utilized in reasonable compliance with the proposal.

Dr. Sakai commented on the board's proposal at § 1753.3(a)(g) to exempt from certain record keeping requirements sterile products compounded on a one-time basis for administration within 72 hours. He states that this proposal falls short of USP 797 guidelines. The board rejects this comment. In the board's proposal, the board does specify that sterile products compounded on a one-time basis for administration with 72 hours would be exempt from the recordkeeping requirements found in that paragraph so long as they are stored in accordance with USP standards. Also, during the 15-day comment, the board proposed modifications to further specify the USP 797 reference to "Redispensed CSPs."

Comments from Maria D. Serpa, PharmD

Dr. Serpa made general comments related to compounded drug products in an acute care setting, and requested that the board's regulations related to sterile-injectable and non-sterile compounding be restructured. Those comments that were not specifically directed at the board's proposed action or to the procedures followed by the board in proposing or adopting the action were rejected.

Dr. Serpa commented in support of the documentation requirements related to batching multiple doses of medications for future use that are not patient specific. The board infers this comment is directed at its proposal to amend § 1735.2(d) which specifies the information that must be included in a written master formula for a compounded drug product. The board appreciates Dr. Serpa's comment.

Dr. Serpa commented in opposition to the board's proposal that the "expiration date" of each component (ingredient) of a compounded drug product be recorded in the pharmacy record. The board disagrees with and rejects this comment because recording the expiration date of each component in a compounded drug product will aid in the proper labeling of the drug product prior to dispensing to a patient. Existing regulation at § 1735.2(h) requires every compounded drug product to be given an expiration date representing the date beyond which the drug product shall not be used. This 'beyond use date' shall not exceed the shortest expiration date of any component in the compounded drug product, with certain exceptions. Thus, the board's proposal to require that the pharmacy record include the expiration date for each component in a compounded drug product will aid in the proper labeling of the drug product. The board also asserts that this requirement provides an added check to prevent expired medication from reaching patients and that it would allow for traceability and accountability for the compounded drug product.

Comments from Rita Shane, PharmD, FASHP, FCSHP and Katherine Palmer, PharmD.

Drs. Shane and Palmer commented on the self-assessment form incorporated by reference at § 1735.2(j) entitled "Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment (Form 17M-39); specifically, Drs. Shane and Palmer recommend that the board clarify the USP reference made at item 3.1.6 related to USP 797. After the 45-day public comment period, the board modified the proposal at § 1735.3(a)(6) to specify "…and stored in accordance with United States Pharmacopeia Standards for "Redispensed CSPs" in Chapter 797 (35th Revision, Effective May 1, 2012). With the adoption of that language following the (15-day) public comment, the board will update the language found at 3.1.6 to reflect the actual language of the regulation, as adopted. The board views this change to Form 17M-39 as non-substantive.

Drs. Shane and Palmer commented on the board's proposal at § 1735.3(a)(6) which requires that the expiration date of each component in a compounded drug product be recorded in the pharmacy record. They state that this documentation will be performed manually and is subject to transcription error. The board disagrees with and rejects this comment (1) because there is no requirement that the information be recorded manually and (2) because recording the expiration date of each component in a compounded drug product will aid in the proper labeling of the drug product prior to dispensing to a patient. Existing regulation at § 1735.2(h) requires every compounded drug product to be given an expiration date representing the date beyond which the drug product shall not be used. This 'beyond use date' shall not exceed the shortest expiration date of any component in the compounded drug product, with certain exceptions. Thus, the board's proposal to require that the pharmacy record include the expiration date for each component in a compounded drug product will aid in the proper labeling of the drug product. The board also asserts that this requirement provides an added check to prevent expired medication from reaching patients and that it would allow for traceability and accountability for the compounded drug product.

Drs. Shane and Palmer commented on the board's proposal at § 1751.2(d) regarding the labeling of cytotoxic agents. Following the 45-day public comment period, and in response to the comment, the board proposed modification to this language so that the label would read

"Cytotoxic – Dispose of Properly." The board did not receive any comments to the modified language during the 15-day comment period for the modified text.

Drs. Shane and Palmer commented on the board's Notice that denoted a search of Title 21 Code of Federal Regulations (Food and Drugs) as well as the Federal Food, Drug and Cosmetic Act (21 U.S.C. 301 et seq.), and stated that on a federal level USP regulatory standards are established in the Food, Drug, and Cosmetic Act and provide direction for safely determining the appropriate beyond use dating of compounded products in hospitals and other healthcare facilities. The board appreciates the comment of Drs. Shane and Palmer and notes that the United States Pharmacopeia standards are not statutes or regulations, but are national standards.

Drs. Shane and Palmer commented on the "Business Impact" portion of the board's Notice, stating that while the board's proposal to amend § 1735.3(a)(6) [allowing sterile products compounded on a one-time basis for administration within 72 hours be stored in accordance with USP standards, as specified] will help, there will still be drug wastage that will result in significant patient care and economic consequences. Drs. Shane and Palmer did not describe what those patient care and economic consequences would be, but they did assert that adoption of national sterile compounding standards (USP 797) would specify a 9 – 14 day (216-335 hour). The board rejected the comment.

Summary of Comments Received During the 15-Day Comment Period for Modified Text (Objections or Recommendations/Responses):

The board received one comment from Therese Beauclair, RPh, during the 15-day public comment period from July 5-20, 2012. Ms. Beauclair's comment, however, is deemed irrelevant (per Government Code §11346.9) and non-responsive because it was not specifically directed at the board's proposed action (modified text) or to the procedures followed by the board.

Summary of Comments Received During the 15-Day Comment Period Regarding the Document Being Added To The Rulemaking Record:

The Board did not receive any comments in response to the document being added to the rulemaking record.

Incorporation by Reference

The board incorporated by reference at 16 Cal.Code Reg. § 1735.2(j) a compounding self-assessment form (Form 17M-39, Rev. 02/12). This is a multi-page document with text, bullets, formatting boxes, etc. The incorporation by reference method was used because it would be impractical and cumbersome to publish the self-assessment form in the California Code of Regulations (CCR). This self-assessment form was developed to promote compliance through self-examination and education. Prior to allowing any drug product to be compounded

in a pharmacy, the pharmacist-in-charge completes the self-assessment. This self-assessment also would be completed before July 1 of every odd-numbered year, within 30 days of the start of a new pharmacist-in-charge, and within 30 days of the issuance of a new pharmacy license. If the self-assessment were incorporated into the CCR, it would increase the size of Division 17 and may cause confusion to the user. The self-assessment was made available to the public and was posted on the board's website.